used to analyse the actin staining of the cells. Control cells which were treated only with the vehicle showed the classical actin distribution. After treatment with 0.1 μM of bpV(pic) and bpV(phen) morphology remains unchanged even after 24 h. Only concentrations as high as 1 and 10 μM over 24 h caused morphological changes. Actin filaments started to re-arrange and cells and nuclei round up. Fibroblasts started to detach and die. These findings indicate that toxicity of the compound starts at μmolar concentrations. scale bar = 10 μm.

Figure 4 **Effect of μmolar bpV(pic) on PKB phosphorylation in the presence of the PI3K inhibitor Ly294002 and the mTOR inhibitor rapamycin:** Resting fibroblasts were pre-incubated with the Ly294002 (10 μM) and rapamycin (50 nM) for 20 min and 30 min, respectively. This was follwed by a treatment with either 10 or 1 μM bpV(pic). The PI3K inhibitor ly294002 dimished bpV(pic) induced PKB phosphorylation. In contrast, mTOR inhibitor rapamycin increased phosphorylation level of PKB.

Figure 5: **Dose dependence of PTEN inhibition, *in vivo*:**

Fig 5a Starved fibroblasts that were incubated with different concentrations of all four bpV compounds for 5 min and stimulated for 15 min with 0.5 μg/ml insulin showed increasing PKB phosphorylation on Western Blots detecting pSer473 in a concentration-dependent manner. Densitometric analysis resulted in *in vivo* IC_{50} values in the lower nano-molar range using NIH Image program.

Fig 5b Similar experiments accomplished in the PTEN-negative cell line UM-UC did not change the phosphorylation level of Ser473 of PKB at the same concentrations